AMENDMENTS TO THE CLAIMS

In the Claims:

Claims 1-69 were previously cancelled and claims 70-226 were previously presented in the Preliminary Amendment filed on December 27, 2001 and amended in the Amendment files April 6, 2005. Please amend claims 70, 101, 132, 163 and 194 to incorporate respectively the limitations of claims 78, 109, 140, 171 and 202 which recited formulating a therapeutic adenovirus composition "which has a BSA content below the detection level of a western blot assay." Those claims have now been amended to recite the requirement that the adenovirus composition be "essentially free of BSA." This amendment is supported in the specification such as at page 72, lines 15-17 [para. 0262] which teaches that the composition should be "essentially free of pyrogens as well as other impurities that could be harmful to humans or animals." In addition, claim 72 which was previously indicated to be free of the art, has been amended to place it in independent form. Claims 73, 104, 166, 196 and 197 have been amended to place them in independent form and claims 103, 134, 135, 165 196 have been amended to place them in independent form while correcting an obvious typographical error in omitting the recitation of "purified." Finally, claim 226 has been amended to correct an obvious typographical error in its designation of dependency.

Claims 1-69 (Cancelled).

70. (Currently Amended) A method of treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition <u>which has a BSA content below the detection level of a western blot assay; and</u>

b) administering said therapeutic adenovirus composition to a patient.

71. (Previously Presented) The method of claim 70, wherein the therapeutic adenovirus comprises 70% +/- 10% of the starting PFU of the lysate of step iv.

72. (Currently Amended) A ~~The~~ method of ~~claim 70~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition, wherein the therapeutic adenovirus comprises a substantially purified therapeutic adenovirus composition; and

b) administering said therapeutic adenovirus composition to a patient.

73. (Currently Amended) A ~~The~~ method of ~~claim 70~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.8 ng/ml; and

b) administering said therapeutic adenovirus composition to a patient.

74. (Previously Presented) The method of claim 70, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.2 ng/ml.

75. (Previously Presented) The method of claim 70, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

76. (Previously Presented) The method of claim 70, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of 1.27 +/- 0.03.

77. (Previously Presented) The method of claim 70, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.8 ng/ml and an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

78. (Currently Amended) The method of claim 70, wherein the therapeutic adenovirus composition is essentially free of BSA ~~has a BSA content below the detection level of a western blot assay~~.

79. (Previously Presented) The method of claim 70, wherein the media is serum-free.

80. (Previously Presented) The method of claim 70, wherein the host cells are grown in a bioreactor.

81. (Previously Presented) The method of claim 70, wherein the host cells are grown on microcarriers.

82. (Previously Presented) The method of claim 70, wherein the host cells are provided nutrients by perfusion.

83. (Previously Presented) The method of claim 70, wherein the host cells are provided nutrients by fed batch.

84. (Previously Presented) The method of claim 70, wherein the host cells are provided nutrients by automated roller bottle.

85. (Previously Presented) The method of claim 70, wherein said therapeutic adenovirus composition comprises an adenoviral vector encoding an exogenous gene construct.

86. (Previously Presented) The method of claim 85, wherein said exogenous gene construct is operatively linked to a promoter.

87. (Previously Presented) The method of claim 86, wherein said promoter is SV40 IE, RSV LTR, β-actin, CMV IE, adenovirus major late, polyoma F9-1, or tyrosinase.

88. (Previously Presented) The method of claim 85, wherein said exogenous gene construct encodes a therapeutic gene.

89. (Previously Presented) The method of claim 88, wherein said therapeutic gene encodes antisense *ras*, antisense *myc*, antisense *raf*, antisense *erb*, antisense *src*, antisense *fms*, antisense *jun*, antisense *trk*, antisense *ret*, antisense *gsp*, antisense *hst*, antisense *bcl*, antisense *abl*, Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-1, MEN II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, GM-CSF, G-CSF, thymidine kinase or p53.

90. (Previously Presented) The method of claim 88, wherein said therapeutic gene encodes p53.

91. (Previously Presented) The method of claim 70, wherein said therapeutic adenovirus composition is a replication-incompetent adenovirus.

92. (Previously Presented) The method of claim 91, wherein said replication-incompetent adenovirus composition is lacking at least a portion of the E1-region.

93. (Previously Presented) The method of claim 91, wherein said replication-incompetent adenovirus composition is lacking at least a portion of the E1A and/or E1B region.

94. (Previously Presented) The method of claim 70, wherein said host cells are capable of complementing replication.

95. (Previously Presented) The method of claim 70, wherein said host cells are 293 cells.

96. (Previously Presented) The method of claim 70, wherein said lysate is treated with a nuclease.

97. (Previously Presented) The method of claim 70, wherein said therapeutic adenovirus composition comprises a pharmaceutically acceptable buffer.

98. (Previously Presented) The method of claim 70, wherein said therapeutic adenovirus comprises a unit dose of between 10^3 and 10^{15} PFU/dose.

99. (Previously Presented) The method of claim 70, wherein said therapeutic adenovirus composition comprises a unit dose of between 10^{10} and 10^{14} PFU/dose.

100. (Previously Presented) The method of claim 70, wherein said patient is a cancer patient.

101. (Currently Amended) A method of treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a bioreactor or on a microcarrier;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition which has a BSA content below the detection level of a western blot assay; and

b) administering said therapeutic adenovirus composition to a patient.

102. (Previously Presented) The method of claim 101, wherein the therapeutic adenovirus comprises 70% +/- 10% of the starting PFU of the lysate of step iv.

103. (Currently Amended) A ~~The~~ method of ~~claim 101, wherein the therapeutic adenovirus comprises~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a bioreactor or on a microcarrier;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a substantially purified therapeutic adenovirus composition; and

b) administering said therapeutic adenovirus composition to a patient.

104. (Previously Presented) A ~~The~~ method of ~~claim 101, wherein the therapeutic adenovirus composition comprises~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a bioreactor or on a microcarrier;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a composition which has a contaminating nucleic acid concentration of less than 0.8 ng/ml and

b) administering said therapeutic adenovirus composition to a patient.

105. (Previously Presented) The method of claim 101, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.2 ng/ml.

106. (Previously Presented) The method of claim 101, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

107. (Previously Presented) The method of claim 101, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of 1.27 +/- 0.03.

108. (Previously Presented) The method of claim 101, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.8 ng/ml and an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

109. (Currently Amended) The method of claim 101, wherein the therapeutic adenovirus composition is essentially free of BSA ~~has a BSA content below the detection level of a western blot assay~~.

110. (Previously Presented) The method of claim 101, wherein the media is serum-free.

111. (Previously Presented) The method of claim 101, wherein the host cells are grown in a bioreactor.

112. (Previously Presented) The method of claim 101, wherein the host cells are grown on microcarriers.

113. (Previously Presented) The method of claim 101, wherein the host cells are provided nutrients by perfusion.

114. (Previously Presented) The method of claim 101, wherein the host cells are provided nutrients by fed batch.

115. (Previously Presented) The method of claim 101, wherein the host cells are provided nutrients by automated roller bottle.

116. (Previously Presented) The method of claim 101, wherein said therapeutic adenovirus composition comprises an adenoviral vector encoding an exogenous gene construct.

117. (Previously Presented) The method of claim 116, wherein said exogenous gene construct is operatively linked to a promoter.

118. (Previously Presented) The method of claim 117, wherein said promoter is SV40 IE, RSV LTR, β-actin, CMV IE, adenovirus major late, polyoma F9-1, or tyrosinase.

119. (Previously Presented) The method of claim 116, wherein said exogenous gene construct encodes a therapeutic gene.

120. (Previously Presented) The method of claim 119, wherein said therapeutic gene encodes antisense *ras*, antisense *myc*, antisense *raf*, antisense *erb*, antisense *src*, antisense *fms*, antisense *jun*, antisense *trk*, antisense *ret*, antisense *gsp*, antisense *hst*, antisense *bcl*, antisense *abl*, Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-1, MEN II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, GM-CSF, G-CSF, thymidine kinase or p53.

121. (Previously Presented) The method of claim 119, wherein said therapeutic gene encodes p53.

122. (Previously Presented) The method of claim 101, wherein said therapeutic adenovirus composition is a replication-incompetent adenovirus.

123. (Previously Presented) The method of claim 122, wherein said replication-incompetent adenovirus composition is lacking at least a portion of the E1-region.

124. (Previously Presented) The method of claim 122, wherein the replication-incompetent adenovirus composition is lacking at least a portion of the E1A and/or E1B region.

125. (Previously Presented) The method of claim 101, wherein said host cells are capable of complementing replication.

126. (Previously Presented) The method of claim 101, wherein said host cells are 293 cells.

127. (Previously Presented) The method of claim 101, wherein said lysate is treated with a nuclease.

128. (Previously Presented) The method of claim 101, wherein said therapeutic adenovirus composition comprises a pharmaceutically acceptable buffer.

129. (Previously Presented) The method of claim 101, wherein said therapeutic adenovirus composition comprises a unit dose of between 10^3 and 10^{15} PFU/dose.

130. (Previously Presented) The method of claim 101, wherein said therapeutic adenovirus composition comprises a unit dose of between 10^{10} and 10^{14} PFU/dose.

131. (Previously Presented) The method of claim 101, wherein said patient is a cancer patient.

132. (Currently Amended) A method of treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells by perfusion or through a fed batch or roller bottle process;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition which has a BSA content below the detection level of a western blot assay; and

b) administering said therapeutic adenovirus composition to a patient.

133. (Previously Presented) The method of claim 132, wherein the therapeutic adenovirus composition comprises 70% +/- 10% of the starting PFU of the lysate of step iv.

134. (Currently Amended) A ~~The~~ method of ~~claim 132~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells by perfusion or through a fed batch or roller bottle process;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus wherein the therapeutic adenovirus composition comprises a substantially purified therapeutic adenovirus composition;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition which has a BSA content below the detection level of a western blot assay; and

b) administering said therapeutic adenovirus composition to a patient.

135. (Currently Amended) A ~~The~~ method of ~~claim 132~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells by perfusion or through a fed batch or roller bottle process;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate to provide therapeutic adenovirus wherein the therapeutic adenovirus composition comprises a substantially purified therapeutic adenovirus composition and has a contaminating nucleic acid concentration of less than 0.8 ng/ml;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition which has a BSA content below the detection level of a western blot assay; and

b) administering said therapeutic adenovirus composition to a patient.

136. (Previously Presented) The method of claim 132, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.2 ng/ml.

137. (Previously Presented) The method of claim 132, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

138. (Previously Presented) The method of claim 132, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of 1.27 +/- 0.03.

139. (Previously Presented) The method of claim 132, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.8 ng/ml and an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

140. (Currently Amended) The method of claim 132, wherein the therapeutic adenovirus composition is essentially free of BSA ~~has a BSA content below the detection level of a western blot assay~~.

141. (Previously Presented) The method of claim 132, wherein the media is serum-free.

142. (Previously Presented) The method of claim 132, wherein the host cells are grown in a bioreactor.

143. (Previously Presented) The method of claim 132, wherein the host cells are grown on microcarriers.

144. (Previously Presented) The method of claim 132, wherein the host cells are provided nutrients by perfusion.

145. (Previously Presented) The method of claim 132, wherein the host cells are provided nutrients by fed batch.

146. (Previously Presented) The method of claim 132, wherein the host cells are provided nutrients by automated roller bottle.

147. (Previously Presented) The method of claim 132, wherein said therapeutic adenovirus composition comprises an adenoviral vector encoding an exogenous gene construct.

148. (Previously Presented) The method of claim 147, wherein said exogenous gene construct is operatively linked to a promoter.

149. (Previously Presented) The method of claim 150, wherein said promoter is SV40 IE, RSV LTR, β-actin, CMV IE, adenovirus major late, polyoma F9-1, or tyrosinase.

150. (Previously Presented) The method of claim 149, wherein said exogenous gene construct encodes a therapeutic gene.

151. (Previously Presented) The method of claim 150, wherein said therapeutic gene encodes antisense *ras*, antisense *myc*, antisense *raf*, antisense *erb*, antisense *src*, antisense *fms*, antisense *jun*, antisense *trk*, antisense *ret*, antisense *gsp*, antisense *hst*, antisense *bcl*, antisense *abl*, Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-1, MEN II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, GM-CSF, G-CSF, thymidine kinase or p53.

152. (Previously Presented) The method of claim 150, wherein said therapeutic gene encodes p53.

153. (Previously Presented) The method of claim 132, wherein said therapeutic adenovirus composition is a replication-incompetent adenovirus.

154. (Previously Presented) The method of claim 153, wherein said replication-incompetent adenovirus composition is lacking at least a portion of the E1-region.

155. (Previously Presented) The method of claim 153, wherein the replication-incompetent adenovirus composition is lacking at least a portion of the E1A and/or E1B region.

156. (Previously Presented) The method of claim 132, wherein said host cells are capable of complementing replication.

157. (Previously Presented) The method of claim 132, wherein said host cells are 293 cells.

158. (Previously Presented) The method of claim 132, wherein said lysate is treated with a nuclease.

159. (Previously Presented) The method of claim 132, wherein said therapeutic adenovirus composition comprises is pharmaceutically acceptable buffer.

160. (Previously Presented) The method of claim 132, wherein said therapeutic adenovirus composition comprises a unit dose of between 10^3 and 10^{15} PFU/dose.

161. (Previously Presented) The method of claim 132, wherein said therapeutic adenoviral composition comprises a unit dose of between 10^{10} and 10^{14} PFU/dose.

162. (Previously Presented) The method of claim 132, wherein said patient is a cancer patient.

163. (Currently Amended) A method of treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:
   i) growing host cells in a media;
   ii) providing nutrients to said host cells;
   iii) infecting said host cells with an adenovirus;
   iv) lysing said host cells by a lysis method other than freeze-thaw to provide a cell lysate;
   v) purifying adenovirus from said cell lysate to provide therapeutic adenovirus;
   vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition <u>which has a BSA content below the detection level of a western blot assay; and</u>

b) administering said therapeutic adenovirus composition to a patient.

164. (Previously Presented) The method of claim 163, wherein the therapeutic adenovirus composition comprises 70% +/- 10% of the starting PFU of the lysate of step iv.

165. (Currently Amended) A ~~The~~ method of ~~claim 163,~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells by a lysis method other than freeze-thaw to provide a cell lysate;

v) purifying adenovirus from said cell lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition wherein the therapeutic adenovirus composition comprises a substantially purified therapeutic adenovirus composition which has a BSA content below the detection level of a western blot assay; and

b) administering said therapeutic adenovirus composition to a patient.

166. (Currently Amended) A ~~The~~ method of ~~claim 163,~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells by perfusion, fed batch or automated roller bottles;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells by a lysis method other than freeze-thaw to provide a cell lysate;

v) purifying adenovirus from said cell lysate to provide therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.8 ng/ml and a BSA content below the detection level of a western blot assay; and

b) administering said therapeutic adenovirus composition to a patient.

167. (Previously Presented) The method of claim 163, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.2 ng/ml.

168. (Previously Presented) The method of claim 163, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

169. (Previously Presented) The method of claim 163, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of 1.27 +/- 0.03.

170. (Previously Presented) The method of claim 163, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.8 ng/ml and an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

171. (Currently Amended) The method of claim 163, wherein the therapeutic adenovirus composition is essentially free of BSA ~~has a BSA content below the detection limit of a western blot assay~~.

172. (Previously Presented) The method of claim 163, wherein the media is serum-free.

173. (Previously Presented) The method of claim 163, wherein the host cells are grown in a bioreactor.

174. (Previously Presented) The method of claim 163, wherein the host cells are grown on microcarriers.

175. (Previously Presented) The method of claim 163, wherein the host cells are provided nutrients by perfusion.

176. (Previously Presented) The method of claim 163, wherein the host cells are provided nutrients by fed batch.

177. (Previously Presented) The method of claim 163, wherein the host cells are provided nutrients by automated roller bottle.

178. (Previously Presented) The method of claim 163, wherein said therapeutic adenovirus composition comprises an adenoviral vector encoding an exogenous gene construct.

179. (Previously Presented) The method of claim 178, wherein said exogenous gene construct is operatively linked to a promoter.

180. (Previously Presented) The method of claim 179, wherein said promoter is SV40 IE, RSV LTR, β-actin, CMV IE, adenovirus major late, polyoma F9-1, or tyrosinase.

181. (Previously Presented) The method of claim 178, wherein said exogenous gene construct encodes a therapeutic gene.

182. (Previously Presented) The method of claim 181, wherein said therapeutic gene encodes antisense *ras*, antisense *myc*, antisense *raf*, antisense *erb*, antisense *src*, antisense *fms*, antisense *jun*, antisense *trk*, antisense *ret*, antisense *gsp*, antisense *hst*, antisense *bcl*, antisense *abl*, Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-1, MEN II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, GM-CSF, G-CSF, thymidine kinase or p53.

183. (Previously Presented) The method of claim 181, wherein said therapeutic gene encodes p53.

184. (Previously Presented) The method of claim 163, wherein said therapeutic adenovirus composition is a replication-incompetent adenovirus.

185. (Previously Presented) The method of claim 184, wherein said replication-incompetent adenovirus composition is lacking at least a portion of the E1-region.

186. (Previously Presented) The method of claim 184, wherein the replication-incompetent adenovirus composition is lacking at least a portion of the E1A and/or E1B region.

187. (Previously Presented) The method of claim 163, wherein said host cells are capable of complementing replication.

188. (Previously Presented) The method of claim 163, wherein said host cells are 293 cells.

189. (Previously Presented) The method of claim 163, wherein said lysate is treated with a nuclease.

190. (Previously Presented) The method of claim 163, wherein said therapeutic adenovirus composition comprises is pharmaceutically acceptable buffer.

191. (Previously Presented) The method of claim 163, wherein said therapeutic adenovirus composition comprises a unit dose of between 10^3 and 10^{15} PFU/dose.

192. (Previously Presented) The method of claim 163, wherein said therapeutic adenovirus composition comprises a unit dose of between 10^{10} and 10^{14} PFU/dose.

193. (Previously Presented) The method of claim 163, wherein said patient is a cancer patient.

194. (Currently Amended) A method of treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate by a method that includes at least one chromatography step, without the use of cesium chloride density gradient centrifugation capable of providing therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide a therapeutic adenovirus composition which has a BSA content below the detection level of a western blot assay; and

b) administering said therapeutic adenovirus composition to a patient.

195. (Previously Presented) The method of claim 194, wherein the therapeutic adenovirus composition comprises 70% +/- 10% of the starting PFU of the lysate of step iv.

196. (Currently Amended) A ~~The~~ method of ~~claim 194,~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate by a method that includes at least one chromatography step, capable of providing therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide ~~wherein the therapeutic adenovirus composition comprises~~ a substantially purified therapeutic adenovirus composition; and

b) administering said therapeutic adenovirus composition to a patient.

197. (Previously Presented) A ~~The~~ method of ~~claim 194,~~ treating a patient with a therapeutic adenovirus composition, comprising:

a) preparing a therapeutic adenovirus composition by a process that includes:

i) growing host cells in a media;

ii) providing nutrients to said host cells;

iii) infecting said host cells with an adenovirus;

iv) lysing said host cells to provide a lysate;

v) purifying adenovirus from said lysate by a method that includes at least one chromatography step, capable of providing therapeutic adenovirus;

vi) formulating said therapeutic adenovirus to provide ~~wherein the therapeutic adenovirus composition~~ has a contaminating nucleic acid concentration of less than 0.8 ng/ml; and

b) administering said therapeutic adenovirus composition to a patient.

198. (Previously Presented) The method of claim 194, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.2 ng/ml.

199. (Previously Presented) The method of claim 194, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

200. (Previously Presented) The method of claim 194, wherein the therapeutic adenovirus composition has an A_{260}/A_{280} ratio of 1.27 +/- 0.03.

201. (Previously Presented) The method of claim 194, wherein the therapeutic adenovirus composition has a contaminating nucleic acid concentration of less than 0.8 ng/ml and an A_{260}/A_{280} ratio of between about 1.2 and 1.3.

202. (Currently Amended) The method of claim 194, wherein the therapeutic adenovirus composition is essentially free of BSA ~~has a BSA content below the detection level of a western blot assay~~.

203. (Previously Presented) The method of claim 194, wherein the media is serum-free.

204. (Previously Presented) The method of claim 194, wherein the host cells are grown in a bioreactor.

205. (Previously Presented) The method of claim 194, wherein the host cells are grown on microcarriers.

206. (Previously Presented) The method of claim 194, wherein the host cells are provided nutrients by perfusion.

207. (Previously Presented) The method of claim 194, wherein the host cells are provided nutrients by fed batch.

208. (Previously Presented) The method of claim 194, wherein the host cells are provided nutrients by automated roller bottle.

209. (Previously Presented) The method of claim 194, wherein said therapeutic adenovirus composition comprises an adenoviral vector encoding an exogenous gene construct.

210. (Previously Presented) The method of claim 209, wherein said exogenous gene construct is operatively linked to a promoter.

211. (Previously Presented) The method of claim 210, wherein said promoter is SV40 IE, RSV LTR, β-actin, CMV IE, adenovirus major late, polyoma F9-1, or tyrosinase.

212. (Previously Presented) The method of claim 209, wherein said exogenous gene construct encodes a therapeutic gene.

213. (Previously Presented) The method of claim 212, wherein said therapeutic gene encodes antisense *ras*, antisense *myc*, antisense *raf*, antisense *erb*, antisense *src*, antisense *fms*, antisense *jun*, antisense *trk*, antisense *ret*, antisense *gsp*, antisense *hst*, antisense *bcl*, antisense *abl*, Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-1, MEN II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, GM-CSF, G-CSF, thymidine kinase or p53.

214. (Previously Presented) The method of claim 212, wherein said therapeutic gene encodes p53.

215. (Previously Presented) The method of claim 194, wherein said therapeutic adenovirus composition is a replication-incompetent adenovirus.

216. (Previously Presented) The method of claim 215, wherein said replication-incompetent adenovirus composition is lacking at least a portion of the E1-region.

217. (Previously Presented) The method of claim 215, wherein the replication-incompetent adenovirus composition is lacking at least a portion of the E1A and/or E1B region.

218. (Previously Presented) The method of claim 194, wherein said host cells are capable of complementing replication.

219. (Previously Presented) The method of claim 194, wherein said host cells are 293 cells.

220. (Previously Presented) The method of claim 194, wherein said lysate is treated with a nuclease.

221. (Previously Presented) The method of claim 194, wherein said therapeutic adenovirus composition comprises is pharmaceutically acceptable buffer.

222. (Previously Presented) The method of claim 194, wherein said therapeutic adenovirus composition comprises a unit dose of between 10^3 and 10^{15} PFU/dose.

223. (Previously Presented) The method of claim 194, wherein said therapeutic adenovirus commission comprises a unit dose of between 10^{10} and 10^{14} PFU/dose.

224. (Previously Presented) The method of claim 194, wherein said patient is a cancer patient.

225. (Previously Presented) The method of claim 194, wherein the chromatography step is a single chromatography step.

226. (Currently Amended) The method of claim 225 ~~230~~, wherein said single chromatography step is anion exchange chromatography.